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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/727,812	11/30/2000	Donald E. Awrey	IPT-003.01	4308

25181 7590 10/07/2003

FOLEY HOAG, LLP
PATENT GROUP, WORLD TRADE CENTER WEST
155 SEAPORT BLVD
BOSTON, MA 02110

EXAMINER	
COUNTS, GARY W	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 10/07/2003

13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/727,812	Applicant(s) AWREY ET AL.	
	Examiner Gary W. Counts	Art Unit 1641	

-- The MAILING DATE of this communication app ars on th cover sh t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *9-15 and 29-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 16-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the claims

The amendment filed July 17, 2003 is acknowledged and has been entered.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1-6, 8, 16, 18-21, 23, 24, 27 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Patterson et al (Application of combined mass spectrometry and partial amino acid sequence to the identification of gel-separated proteins, electrophoresis 1996, 17, p877-891) in view of Formosa et al (Using Protein Affinity Chromatography to Probe Structure of Protein Machines", Methods in Enzymology 208: 24-45, (1991)).

Patterson et al disclose exposing a cell lysate to an affinity column having a protein ligand immobilized to a matrix. Patterson et al disclose that this ligand can be a fusion protein (p 878). Patterson et al disclose eluting the column and subjecting the eluted proteins to gel electrophoresis. Patterson et al disclose digesting the proteins and analyzing the protein by mass spectrometry to identify the protein (abstract and see also figure on page 880).

Patterson et al differ from the instant invention in failing to teach two or more columns having a protein ligand in varying concentrations immobilized to a matrix and also fails to teach the ligand is covalently bound to the matrix.

Formosa et al disclose the use of multiple microaffinity columns having a ligand immobilized to a matrix in varying concentrations (pages 36-37). Formosa et al disclose preparing the columns and coupling the protein ligand to the matrix. Formosa et al also disclose covalently immobilizing the protein ligand to the matrix. Formosa et al disclose the importance of purifying the protein ligand (p. 26) Formosa et al disclose that the use of such affinity columns allows for the dissociation constants of the protein-protein interactions to be estimated and also provides the advantage to screen for the effects of a variety of conditions on the binding of proteins from extracts (page 35).

It would have been obvious to one of ordinary skill in the art to incorporate multiple affinity columns having a protein ligand in varying concentrations immobilized to a matrix such as taught by Formosa et al into the method of Patterson et al because Formosa et al shows that the use of such affinity columns allows for the dissociation constants of the protein-protein interactions to be estimated and also provides the advantage to screen for the effects of a variety of conditions on the binding of proteins from extracts. Further, it also would have been obvious to one of ordinary skill in the art to covalently immobilize the protein ligand to the matrix as taught by Formosa et al because Formosa et al teaches that such immobilization provides for sensitive detection of protein-protein interaction and to achieve optimal sensitivity (page 25).

Patterson et al in view of Formosa et al teaches the claimed invention except for teaching the protein-affinity chromatography is an automated process. It would have been obvious to one having ordinary skill in the art at the time the invention was made to automate the protein-affinity chromatography, since it has been held that broadly providing a mechanical or automatic means to replace manual activity, which has accomplished the same result, involves only routine skill in the art. *In re Venner,* 120 USPQ 192.

3. Claims 7, 17, 22, 25 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Patterson et al in view of Formosa et al as applied to claims 1-6, 8, 16, 18-21, 23, 24, 27 and 28 above, and further in view of Vestal et al (US 6,281,493). See above for teachings of Patterson et al and Formosa et al.

Patterson et al and Formosa et al differ from the instant invention in failing to teach the mass spectrometry is MALDI-TOF mass spectrometry.

Vestal et al disclose the use of MALDI-TOF for measuring the mass-to-charge ratio of a sample molecule. Vestal et al disclose that TOF mass spectrometers are advantageous because they are relatively simple, inexpensive instruments with virtually unlimited mass-to-charge range. Vestal et al also disclose that TOF mass spectrometers have potentially higher sensitivity than scanning instruments because they can record all the ions generated from each ionization event (col 1, lines 23-46).

It would have been obvious to one of ordinary skill in the art to incorporate the use of MALDI-TOF mass spectrometry as taught by Vestal et al into the modified method of Patterson et al because Vestal et al teaches that TOF mass spectrometers

are advantageous because they are relatively simple, inexpensive instruments with virtually unlimited mass-to-charge range. Vestal et al also disclose that TOF mass spectrometers have potentially higher sensitivity than scanning instruments because they can record all the ions generated from each ionization event.

With respect to the multiple micro-columns arranged into an array format as recited in the instant claims. Patterson et al in view of Formosa et al disclose the claimed invention except for the micro-columns arranged in an array format. It would have been obvious to one having ordinary skill in the art at the time the invention was made to arrange the micro-columns into an array format, since it has been held that rearranging parts of an invention involves only routine skill in the art. *In re Japikse,* 86 USPQ 70.

With respect to the concentration of the protein ligand bound to the matrix and to the purity of the protein ligand as recited in the instant claims, the optimum concentration of the protein ligand and the purity of the protein ligand bound to the columns can be determined by routine experimentation and thus would have been obvious to one of ordinary skill in the art. Further, it has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454,456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. At 458,105 USPQ at 236-237. The "discovery

of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272,276, 205 USPQ 215, 218-219 (C.C.P.A. 1980).

Response to Arguments

4. Applicant's arguments filed July 17,2003 have been fully considered but they are not persuasive.

Applicant argues that Formosa et al does not teach or suggest that the use of two or more columns with varying ligand concentrations would be useful for isolation and/or identification of an interacting protein. This is not found persuasive because Examiner has not relied upon Formosa for teaching the identification of an interacting protein but rather has relied upon Patterson for this teaching. Further, Formosa et al teaches the characterization of interacting proteins and therefore is considered to be analogous art.

Applicant argues that Formosa et al. does not teach or suggest that the amount of the interacting protein eluting from the columns varies proportionately with the concentration of immobilized protein ligand. Applicant directs Examiners attention to Figure 1A on page 36. Applicant states that based on the figure, it would not be obvious to one of ordinary skill in the art that the amount of the interacting protein eluting from the columns varies proportionately with the concentration of immobilized protein ligand. Applicant states that lanes d and h both have 10 ug of ligand immobilized on the column, but the amount of RAP38 eluted from the column appears to vary significantly. This is not found persuasive because lanes d and h were prepared by different processing procedures. For example, lane d was inactivated in buffer for 30

or 60 minutes before the addition of RNA polymerase II and lane h was not prepared in this manner. Applicant further states that lanes f (ug of immobilized protein) and lane h (10 ug of immobilized protein) would appear to show the same amount of eluted RAP38 even though the concentration ligand immobilized on the column varies by almost two-fold. This is not found persuasive because lanes f and h were prepared by different processing procedures. For example, lane f was inactivated in buffer for 30 or 60 minutes before the addition of RNA polymerase II and lane h was not prepared in this manner. Further, in procedures which were processed in the same manner (see Figure 1A) Formosa shows that RAP38 eluted from the column varies proportionately with the concentration of immobilized ligand. For example, lanes a (0 ug of immobilized protein) shows 0 RAP38 and lane b (20 ug of immobilized protein) shows a significant amount of RAP38. Therefore, it is Examiner's position that Formosa et al teaches the amount of the interacting protein eluting from the columns varies proportionately with the concentration of immobilized ligand.

Applicant argues that Patterson et al. in view of Formosa et al. fail to teach or suggest the currently claimed embodiment and Vestal et al. fail to make up for the deficiencies of Patterson et al. and Formosa et al. This is not found persuasive because it is the Examiner's position that Patterson et al. in view of Formosa et al do teach the currently claimed embodiment and therefore the combination with Vestal is considered appropriate.

Conclusion

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (703) 305-1444. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gary W. Counts

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

10/26/05

Examiner
Art Unit 1641
October 1, 2003